Remarks

Claims 1-28 are presently under examination in this application. Applicants note the withdrawal of the previous objections and rejections, with the exceptions noted below. Claims 1 and 16 have been amended.

Amendments

The paragraph at page 1, line 21 has been amended to correct the spelling of the word "toxoiding."

Claims 1 and 16 have been amended to indicate that the formulation comprises purified botulinum toxin. Support for this amendment may be found at, for example, page 11, line 11 through page 12, line 21. Claim 16 has been further amended to delete the word "liquid" before the word "buffer. Support for this amendment may be found, for example, at page 3, lines 24-26."

Applicants submit that no new matter has been added by these amendments.

Objection to the Specification

The specification stands objected because of a misspelling at page 1, line 23. The specification has been amended as noted above to correct this misspelling. Accordingly, it is submitted that this objection is now moot and Applicants respectfully request that it be withdrawn.

Rejection under 35 U.S.C. 112, First paragraph

Claims 1-28 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enablement to allow claims to a pharmaceutical formulation comprising a botulinum toxin other than type B. This rejection is respectfully traversed. As noted above, Claims 1 and 16 have been amended to include the limitation that the botulinum toxin is a purified botulinum toxin.

The Office Action states that the teaching of the Prevot reference are relevant because Applicant's botulinum toxin (as recited prior to the above-noted amendments) is not a "purified" toxin. It is further stated that Prevot teaches the unpredictability factor by stating that toxin E sometimes behaves like groups A and B botulinum toxins and sometimes like groups C and D toxins with regard to the preservation at +4° C. This reference also reflects batch-to-batch inconsistency in the stability of different botulinum toxins when stored at +4° C at a pH between 5-6.

Claims 1 and 16 have been amended to recite that the botulinum toxin is a "purified botulinum toxin." As noted in Applicant's previous Reply, it is submitted that the Prevot reference is not useful in making an assessment of the state of the art as it was understood at the time this invention was made. Prevot may have taught the state of the art in 1953, however, one skilled in the art would not have recognized Prevot as teaching the state of the art at the time this invention was made. At the time Prevot was published, the purification techniques to remove other cell components from the toxin was neither consistent nor adequate. The state of the art at the time this invention was made recognized the need for rigorous purification of toxin from other cellular contaminants, such as proteases, which can attack and destroy the peptidic chains of the toxin. It is asserted that the unpredictability postulated by the Examiner, based on a reading of Prevot, is largely due to the contamination of the toxin due to the poor purification technologies available at that time.

Applicants have provided extensive teaching regarding the purification of toxin in preparing it for formulation into the stable formulations. Purification of types A and B are described in detail in section III of the specification beginning at about page 10, line 22. As noted at page 12, line 22, toxin types C_1, C_2, D, E, F, or G may be prepared and purified according to methods known in the art. One skilled in the art would understand how to adapt the disclosed methods to provide stable formulations comprising types C – G from reading the specification and references available prior to the filing of this application.

Accordingly, it is submitted that the specification provides adequate disclosure and guidance to enable the currently pending claims. Withdrawal of this rejection is respectfully requested.

Conclusion

For the reasons set forth above, Applicants submit that case is now in condition for allowance. Early notice to that effect is respectfully solicited.

Respectfully submitted,

Date: 2/4/02

SIGNATURE OF PRACTITIONER

Leslie J. Boley
Registration No. 41,490
Elan Pharmaceuticals, Inc.
800 Gateway Boulevard
S. San Francisco, CA 94080
Tel. no. 650-866-2773

Customer no. 21835

MARKED-UP VERSION SHOWING AMENDMENTS

In the Specification:

At Page 1, line 21:

Hambleton, P., Capel, B., Bailey, N., Heron, N.I., Crooks, Al, Melling, J. (1981) Production, purification and toxoiding **[toxoiing]** of *Clostridium botulinum* type A toxin. *Biomedical Aspects of Botulism*, Academic Press, NY.

In the Claims:

--1. (amended) A stable liquid pharmaceutical botulinum toxin formulation, comprising

a pharmaceutically acceptable buffer capable of providing a buffered pH range between about pH 5 and pH 6, and

[isolated**]** **purified** botulinum toxin;

wherein said formulation is stable as a liquid for at least one year at a temperature between about 0 and 10 degrees centigrade.

16. (amended) A stable liquid pharmaceutical botulinum toxin formulation, comprising

a pharmaceutically acceptable **[**liquid**]** buffer capable of providing a buffered pH range between about pH 5 and pH 6, and

[isolated**]** **purified** botulinum toxin;

wherein said toxin formulation is stable as a liquid for at least about 6 months at a temperature between about 10 and 30 degrees centigrade.--